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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,468	07/02/2003	Jingwu Z. Zang	057186.000003	5234

7590 05/24/2006

Attention: J. Wendy Davis, Ph.D.
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EXAMINER	
JUEDES, AMY E	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,468	ZANG ET AL.	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-9,12 and 15-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11,13,14 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/14/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group IV, drawn to isolated peptides, vaccines, and pharmaceutical compositions thereof, claims 10-11, 13-14, and 42-44, in the reply filed on 4/13/06 is acknowledged. Applicant has further elected SEQ ID NO: 4 as the species of peptide.

Applicant's traversal is on that it would not be an undue burden to search for all the species of peptide, since a search for a BV16 TCR encompasses all four peptides. This is not found to be persuasive because the instant claims are not limited to BV16 TCR. For example, claim 10 is drawn an isolated peptide having the amino acid sequence of SEQ ID NO:4, SQD, SLL, or SEQ ID NO: 5. Therefore, separate searches are required for all of the different peptide species. It is an undue burden to perform a separate search for each of the peptides.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9, 12, and 15-41 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 10-11, 13-14 and 42-44 read on the elected invention and are being acted upon.

2. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code on pg. 18. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP §608.01.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 13 and 42-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that Applicant was in possession of the genus of peptides "derived from" a CDR3 region or from a single chain T cell receptor variable region, or "fragments thereof".

The instant claims encompass a broad genus of peptides that might be derived from any T cell receptor BV14 or BV16 T cell receptor. Since every T cell comprises a unique CDR3 region, the genus of peptides encompassed by the claims is extremely large. Furthermore, peptides "derived from" a CDR3 region also encompass a virtually unlimited number of substitutions, deletions, or additions to the CDR3 peptides. Furthermore, said peptides will all comprise unique sequences, and are thus structurally different. Furthermore, claim 42 is not even limited to a CDR3 peptide, and encompasses any peptide derived from any portion of a TCR that comprises BV14 or BV16. Furthermore, Claim 42 encompasses "fragments" of the peptides, which might include just 2 amino acid residues. Applicant's disclosure of several related CDR3 peptides cannot be considered adequate for the virtually unlimited number of structurally different peptides encompassed by the claims. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

5. Claims 13-14 and 42-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the vaccine or pharmaceutical composition comprising a peptide "derived from" a CDR3 or TCR could function to suppress pathogenic T cell responses, as broadly claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art,

the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

With regards to the instant claims, their breadth comprises a primary issue as regards the unpredictability of the claimed method. Claim 42 is drawn to a pharmaceutical composition for suppressing pathogenic T cell responses in vivo. Likewise, Claim 13 is drawn to a vaccine, which encompasses the claimed peptides to suppress pathogenic T cell responses in vivo. Furthermore, the claims encompass vaccines or compositions comprising any peptide "derived from" a CDR3 of a BV14 or BV16 TCR from an individual suffering from rheumatoid arthritis. While it is known that some peptides that closely resemble a potentially pathogenic TCR fragment are useful in treating autoimmune disease (see Vandenbark et al., pg. 714), the instant claims encompass, in their breadth, CDR3 peptides from any BV14 or BV16 TCR, including normal non-pathogenic TCRs. Furthermore, Claim 42 is not even limited to CDR3 peptides, and might encompass any peptide "derived from" a BV14 or BV16 TCR, including those derived from healthy individuals. Since the mechanisms of action of TCR peptide vaccination requires the induction of regulatory T cells that specifically recognize the

TCR of the pathogenic T cells (See Vandenbark, pg. 715), it is not likely that not any CDR3 peptide from any TCR will be capable of suppressing a pathogenic T cell response, as claimed. Furthermore, the instant claims are drawn to a peptide "derived from" a CDR3 region. This encompasses a virtually unlimited number of amino acid substitutions, deletions, or additions to the CDR3 peptide. Since changing the TCR contact resides of peptides can dramatically effect the T cell response (see Janeway and Travers, pg. 4:44), it seems unlikely that all peptides comprising amino acid substitutions or deletions would be able to function to suppress a pathogenic response. Furthermore, even when the claims are limited to peptides comprising a particular amino acid sequence, this still encompasses a broad genus of peptides. For example, some of the peptides only comprise three defined amino acids (SLS, SQD, or SLL). However, Vandenbark et al. teach that not all CDR3 sequences used for vaccination, which range form 8-15 amino acids, contain relevant MHC binding motifs. Therefore, it seems unlikely that all CDR3 peptides which comprise only the amino acid residues SLS, SQD, or SLL would be capable of binding MHC and mediating an in vivo effect. Thus, given the state of the art, the instant specification must provide a sufficient and enabling disclosure, commensurate in scope with the claims. However, the instant specification does not provide any data with regard to the ability of any CDR3 peptides to suppress pathogenic T cell responses. Therefore, given the state of the art and the lack of working examples, the instant invention must be considered highly unpredictable and would require undue experimentation to function as a vaccine or pharmaceutical composition, as claimed.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 10-11 and 13-14 are rejected under 35 U.S.C. 102(a) as being anticipated by GenPept Accession number CAD67333, Feb. 2003, as evidence by Oxford University Press, "peptide" definition.

The CAD67333 reference teaches an amino acid sequence having the amino acid sequence of SEQ ID NO: 4 of the instant application (see residues 92-98 in particular). Since the Oxford dictionary defines a peptide as any compound with two or more amino acids linked together, the sequence taught by CAD67333 is a peptide. It is noted that claims 11 and 13-14 are included since the patentability of a product does not depend on its method of production. Therefore, the fact that the instant peptide is derived from the CDR3 region does not render it patentably distinct from the peptide taught by CAD67333. CAD67333 has taught a peptide identical in structure to the instantly claimed peptide. Furthermore, the term "vaccine" is directed toward an intended use of the peptide, and carries little patentable weight in the absence of evidence of a structural difference.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over CAD67333, Feb. 2003, in view of Cleland et al., 1993.

The teachings of CAD67333 are described above.

CAD67333 does not teach a composition comprising a pharmaceutically acceptable carrier.

Cleland et al. teach that protein formulations containing buffer components and excipients prevent the formation of aggregates that can cause altered half-life (see pg. 317 in particular). Cleland et al. further teaches that the excipients can range form salts to surfactants, including those used in pharmaceutical formulations (i.e. pharmaceutically acceptable), see pg. 317 and 319 in particular.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to

make a formulation comprising the protein taught by CAD67333 and a pharmaceutically acceptable excipients, as taught by Cleland et al. The ordinary artisan at the time the invention was made would have been motivated to do so, and have a reasonable expectation of success, since Cleland et al. teach that protein formulations containing buffers and excipients (including pharmaceutically acceptable excipients) prevent the formation of aggregates that can cause altered half-life.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 3, 2006

5/12/06
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